



US010329536B2

(12) **United States Patent**  
**Vorlop et al.**

(10) **Patent No.:** US 10,329,536 B2  
(b) **Date of Patent:** Jun. 25, 2019

(54) **METHODS FOR PRODUCING AN ACTIVE CONSTITUENT OF A PHARMACEUTICAL OR A DIAGNOSTIC AGENT IN AN MDCK CELL SUSPENSION CULTURE**

(75) Inventors: **Jürgen Vorlop**, Marburg (DE);  
**Christian Frech**, Mannheim (DE);  
**Holger Lübben**, Wetter (DE);  
**Jens-Peter Gregersen**, Wetter (DE)

(73) Assignee: **Seqirus UK Limited**, Berkshire (GB)

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 177 days.

(21) Appl. No.: **10/487,707**

(22) PCT Filed: **Sep. 11, 2002**

(86) PCT No.: **PCT/EP02/10208**

§ 371 (c)(1),  
(2), (4) Date: **Jan. 18, 2005**

(87) PCT Pub. No.: **WO03/023021**

PCT Pub. Date: **Mar. 20, 2003**

(65) **Prior Publication Data**

US 2005/0118140 A1 Jun. 2, 2005

(30) **Foreign Application Priority Data**

Sep. 12, 2001 (DE) ..... 101 44 906

(51) **Int. Cl.**

**C12N 7/00** (2006.01)  
**C12N 5/00** (2006.01)  
**A61K 39/00** (2006.01)

(52) **U.S. Cl.**

CPC ..... **C12N 7/00** (2013.01); **A61K 39/00** (2013.01); **A61K 2039/5252** (2013.01); **C12N 2710/10051** (2013.01); **C12N 2710/16651** (2013.01); **C12N 2710/16751** (2013.01); **C12N 2710/24151** (2013.01); **C12N 2720/12051** (2013.01); **C12N 2720/12351** (2013.01); **C12N 2760/16251** (2013.01); **C12N 2760/18051** (2013.01); **C12N 2760/18551** (2013.01); **C12N 2760/20151** (2013.01); **C12N 2770/24151** (2013.01); **Y02A 50/386** (2018.01); **Y02A 50/388** (2018.01); **Y02A 50/39** (2018.01); **Y02A 50/464** (2018.01); **Y02A 50/466** (2018.01)

(58) **Field of Classification Search**

USPC ..... 435/239, 350, 383  
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,064,232 A	12/1977	Bachmayer et al.
4,500,513 A	2/1985	Brown et al.
4,525,349 A	6/1985	Montagnon et al.
4,783,411 A	11/1988	Gabliks

RE33,164 E	2/1990	Brown et al.
5,013,663 A	5/1991	Acree et al.
5,753,489 A	5/1998	Kistner et al.
5,756,341 A	5/1998	Kistner et al.
5,762,939 A	6/1998	Smith et al.
5,911,998 A	6/1999	Potash et al.
6,455,298 B1	2/2002	Groner et al.
6,514,502 B1	2/2003	Francis
6,656,720 B2	12/2003	Groner et al.
8,506,966 B2	8/2013	Podda et al.
2004/0223976 A1	11/2004	Bianchi et al.
2006/0147477 A1	7/2006	Cabezon Silva et al.
2006/0263386 A1	11/2006	Buschle et al.
2009/0220546 A1	9/2009	Podda et al.
2010/0010199 A1	1/2010	Tsai et al.
2010/0189741 A1	7/2010	Ballou et al.
2011/0045022 A1	2/2011	Tsai
2013/0004942 A1	1/2013	Stohr et al.

FOREIGN PATENT DOCUMENTS

EP	0 019 218	11/1980
EP	00/19218	11/1980
EP	0389925	12/1995
EP	1260581	11/2002
EP	0891420	2/2005
EP	0833933	9/2005
GB	1070764	6/1965
WO	WO91/09937	7/1991

(Continued)

OTHER PUBLICATIONS

Palache et al. Immunogenicity and reactogenicity of influenza subunit vaccines produced in MDCK cells or fertilized chicken eggs 1997. The Journal of Infectious Disease vol. 176, Supplement 1, p. S20-S23.\*

Johnson. Serum-Free Systems for MDBK and MDCK Epithelial Cells Jan. 2001. Sigma-Aldrich Corporation, Life Science Quarterly, vol. 2, Issue 1.\*

Merten et al. The new medium MDSS2N, free of any animal protein supports cell growth and production of various viruses 1999. Cytotechnology vol. 30, p. 191-201.\*

Wrin et al. Adaptation of persistent growth in the H9 cell line renders a primary isolate of human immunodeficiency virus type 1 sensitive to neutralization by vaccine sera. The Journal of Virology, Jan. 1995, vol. 69, No. 1, pp. 39-48.\*

(Continued)

Primary Examiner — Nianxiang Zou

(74) Attorney, Agent, or Firm — Finnegan, Henderson, Farabow, Garrett & Dunner, LLP

(57) **ABSTRACT**

The present invention concerns a method for production of an active ingredient of a drug or diagnostic agent, in which

- (a) MDCK cells are infected with a virus; and
- (b) the MDCK cells are cultured in suspension culture on a commercial scale under conditions that permit multiplication of the viruses;

in which culturing occurs in a volume of at least 30 L.

The invention also concerns a method for production of a drug or diagnostic agent in which an active ingredient is produced according to the above method and mixed with an appropriate adjuvant, auxiliary, buffer, diluent or drug carrier.